



## POMT2 gene

protein O-mannosyltransferase 2

### Normal Function

The *POMT2* gene provides instructions for making one piece of the protein O-mannosyltransferase (POMT) enzyme complex. The other piece is produced from the *POMT1* gene. This enzyme complex is present in many different tissues in the body but is particularly abundant in the muscles used for movement (skeletal muscles), fetal brain, and testes.

The POMT complex helps modify a protein called alpha ( $\alpha$ )-dystroglycan. Specifically, this complex adds a sugar molecule called mannose to  $\alpha$ -dystroglycan through a process called glycosylation. Glycosylation is critical for the normal function of  $\alpha$ -dystroglycan.

The  $\alpha$ -dystroglycan protein helps anchor the structural framework inside each cell (cytoskeleton) to the lattice of proteins and other molecules outside the cell (extracellular matrix). In skeletal muscles, glycosylated  $\alpha$ -dystroglycan helps stabilize and protect muscle fibers. In the brain, it helps direct the movement (migration) of nerve cells (neurons) during early development.

### Health Conditions Related to Genetic Changes

limb-girdle muscular dystrophy

Walker-Warburg syndrome

At least eight mutations in the *POMT2* gene have been found to cause Walker-Warburg syndrome. This condition is the most severe form of a group of disorders known as congenital muscular dystrophies. Walker-Warburg syndrome causes muscle weakness and abnormalities of the brain and eyes. Because of the severity of the problems caused by this condition, affected individuals usually do not survive past early childhood.

*POMT2* gene mutations that cause Walker-Warburg syndrome lead to the formation of nonfunctional POMT enzyme complexes that cannot transfer mannose to  $\alpha$ -dystroglycan, preventing its normal glycosylation. As a result,  $\alpha$ -dystroglycan can no longer effectively anchor cells to the proteins and other molecules that surround them. Without functional  $\alpha$ -dystroglycan to stabilize the muscle fibers, they become

damaged as they repeatedly contract and relax with use. The damaged fibers weaken and die over time, which affects the development, structure, and function of skeletal muscles in people with Walker-Warburg syndrome.

Defective  $\alpha$ -dystroglycan also affects the migration of neurons during the early development of the brain. Instead of stopping when they reach their intended destinations, some neurons migrate past the surface of the brain into the fluid-filled space that surrounds it. Researchers believe that this problem with neuronal migration causes a brain abnormality called cobblestone lissencephaly, in which the surface of the brain lacks the normal folds and grooves and instead appears bumpy and irregular. Less is known about the effects of *POMT2* gene mutations in other parts of the body.

### other disorders

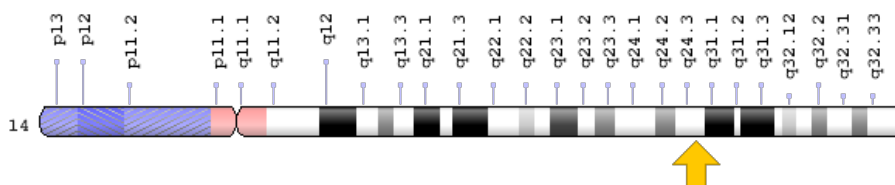
Mutations in the *POMT2* gene are also involved in less severe forms of muscular dystrophy, including muscle-eye-brain disease and *POMT2*-related congenital muscular dystrophy (also known as MDDGB2). Muscle-eye-brain disease is similar to Walker-Warburg syndrome (described above), although affected individuals usually survive into childhood or adolescence. *POMT2*-related congenital muscular dystrophy causes muscle weakness, brain abnormalities, and intellectual disability, but usually does not affect the eyes.

*POMT2* gene mutations that cause these conditions result in POMT enzyme complexes with reduced function. As a result, glycosylation of  $\alpha$ -dystroglycan is impaired. The severity of the resulting condition appears to be related to the level of  $\alpha$ -dystroglycan glycosylation; the less glycosylation, the more severe the condition.

### Chromosomal Location

Cytogenetic Location: 14q24.3, which is the long (q) arm of chromosome 14 at position 24.3

Molecular Location: base pairs 77,274,956 to 77,320,885 on chromosome 14 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- dolichyl-phosphate-mannose--protein mannosyltransferase 2
- LGMD2N
- MDDGA2
- MDDGB2
- MDDGC2
- POMT2\_HUMAN
- protein O-mannosyl-transferase 2
- protein-O-mannosyltransferase 2

## Additional Information & Resources

### Educational Resources

- Molecular Cell Biology (fourth edition, 2000): Protein Glycosylation in the ER and Golgi Complex  
<https://www.ncbi.nlm.nih.gov/books/NBK21744/>
- Washington University Neuromuscular Disease Center  
<http://neuromuscular.wustl.edu/syncm.html#pomt2ww>

### GeneReviews

- Congenital Muscular Dystrophy Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1291>
- Limb-Girdle Muscular Dystrophy Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1408>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28POMT2%5BTIAB%5D%29+OR+%28protein-O-mannosyltransferase+2%5BTIAB%5D%29%29+OR+%28LGMD2N%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2160+days%22%5Bdp%5D>

## OMIM

- MUSCULAR DYSTROPHY-DYSTROGLYCANOPATHY (CONGENITAL WITH MENTAL RETARDATION), TYPE B, 2  
<http://omim.org/entry/613156>
- PROTEIN O-MANNOSYLTRANSFERASE 2  
<http://omim.org/entry/607439>

## Research Resources

- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=POMT2%5Bgene%5D>
- HGNC Gene Family: Dolichyl D-mannosyl phosphate dependent mannosyltransferases  
<http://www.genenames.org/cgi-bin/genefamilies/set/430>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=19743](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=19743)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/29954>
- UniProt  
<http://www.uniprot.org/uniprot/Q9UKY4>

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